Coarse Graining data-driven cellular models in multiscale simulations

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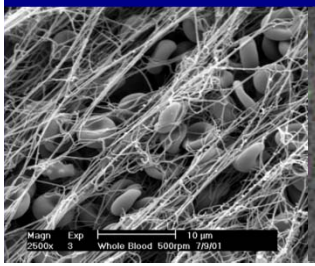

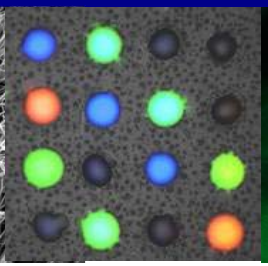

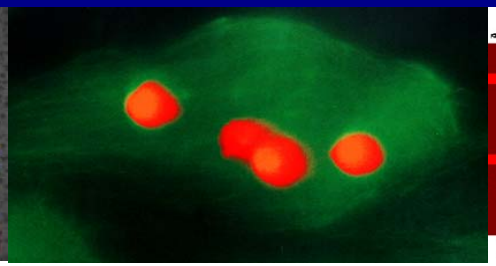

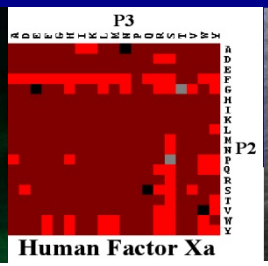

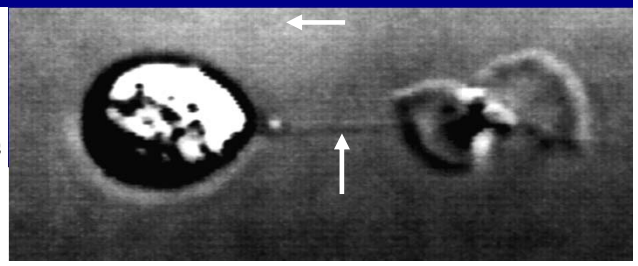

INSTITUTE FOR MEDICINE AND ENGINEERING
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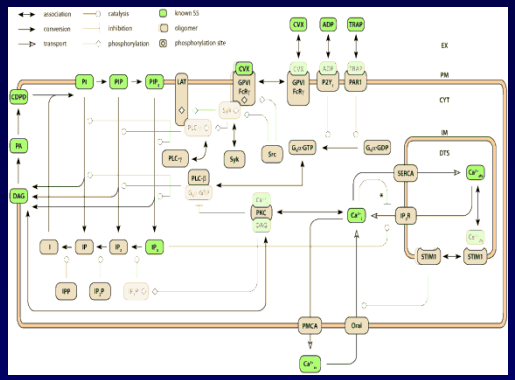
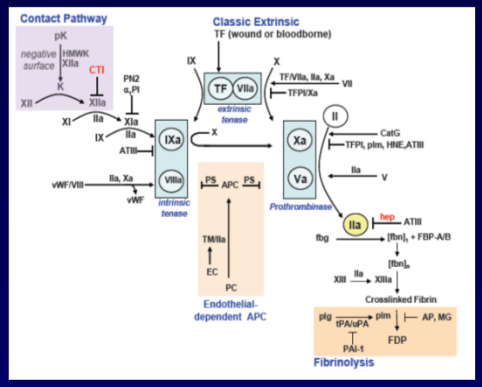
PENN CENTER FOR MOLECULAR DISCOVERY

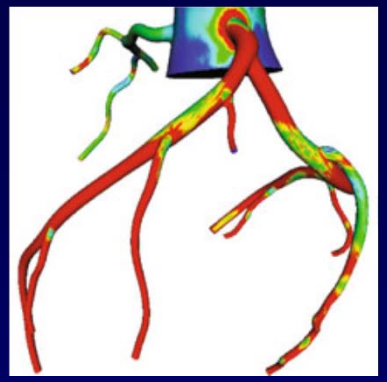
Penn Engineering

blood systems biology

Blood Systems Biology







C. Taylor Lab (Stanford)

Physics

diffusion
velocity
pressure
bond strengths
VWF mechanics
geometry

Parameters

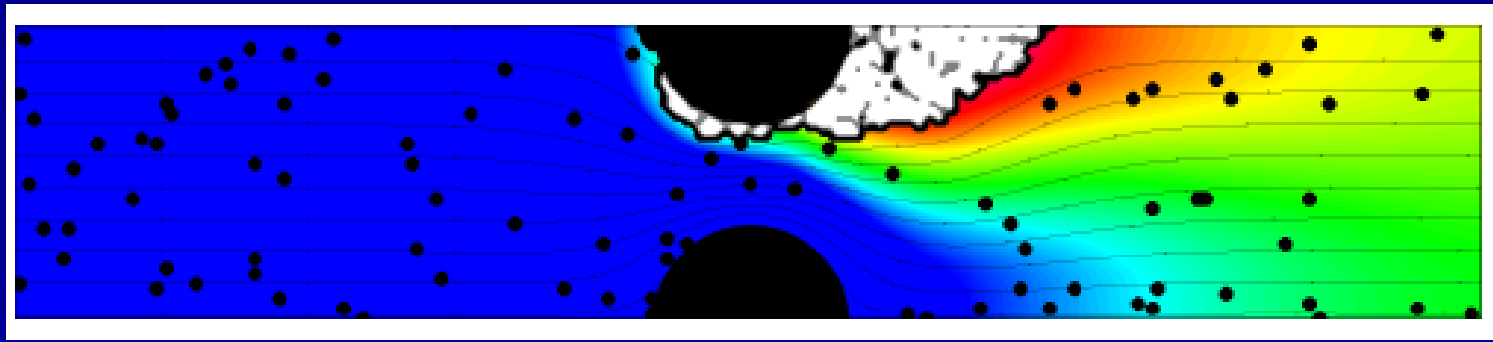
kinetic constants k_i
initial conditions $c_i(0)$

Topology

interaction networks
- nodes and linkages
reaction type

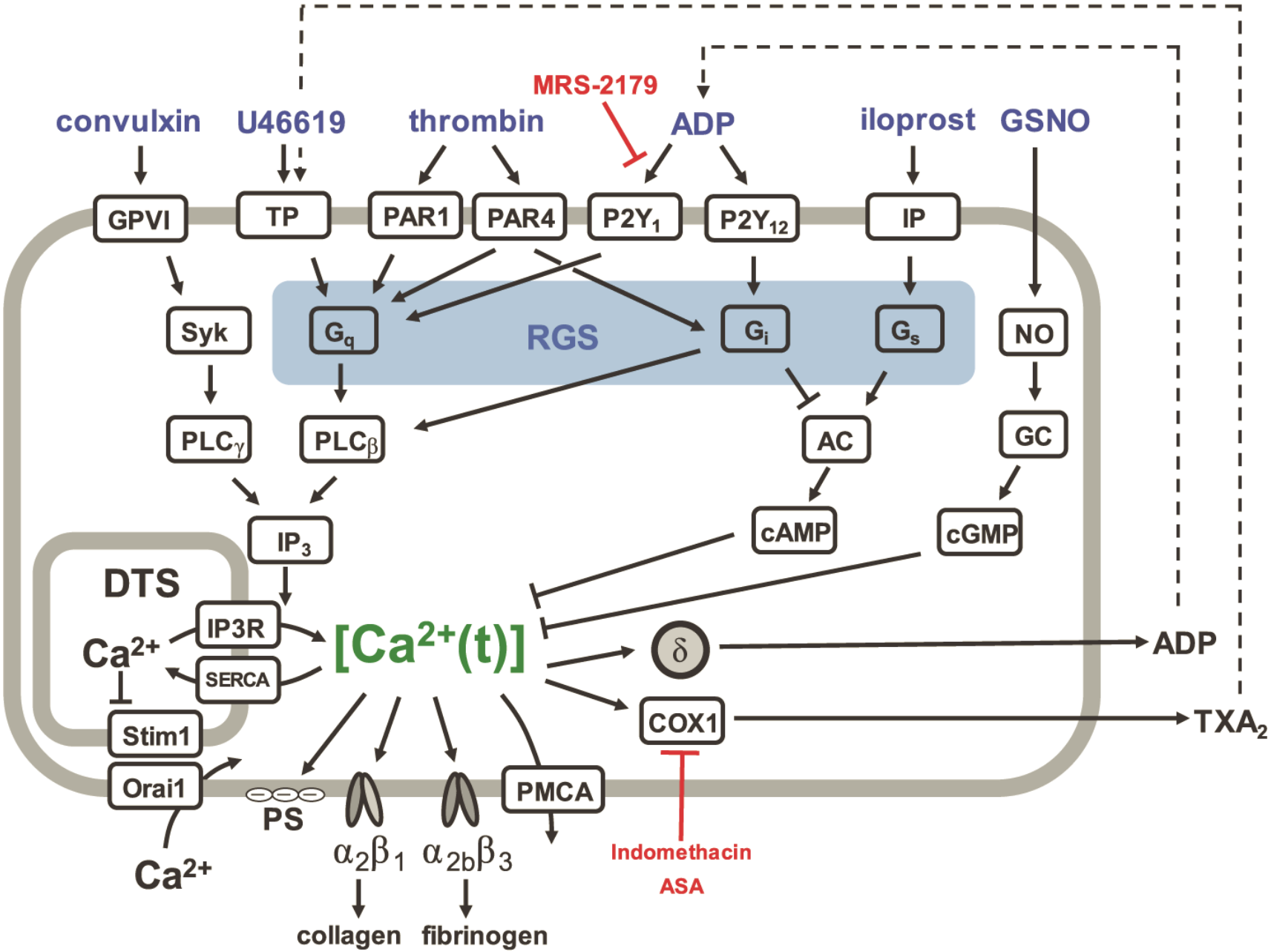
Numerics:

CFD/LB
NN/ODE
LKMC/PDE

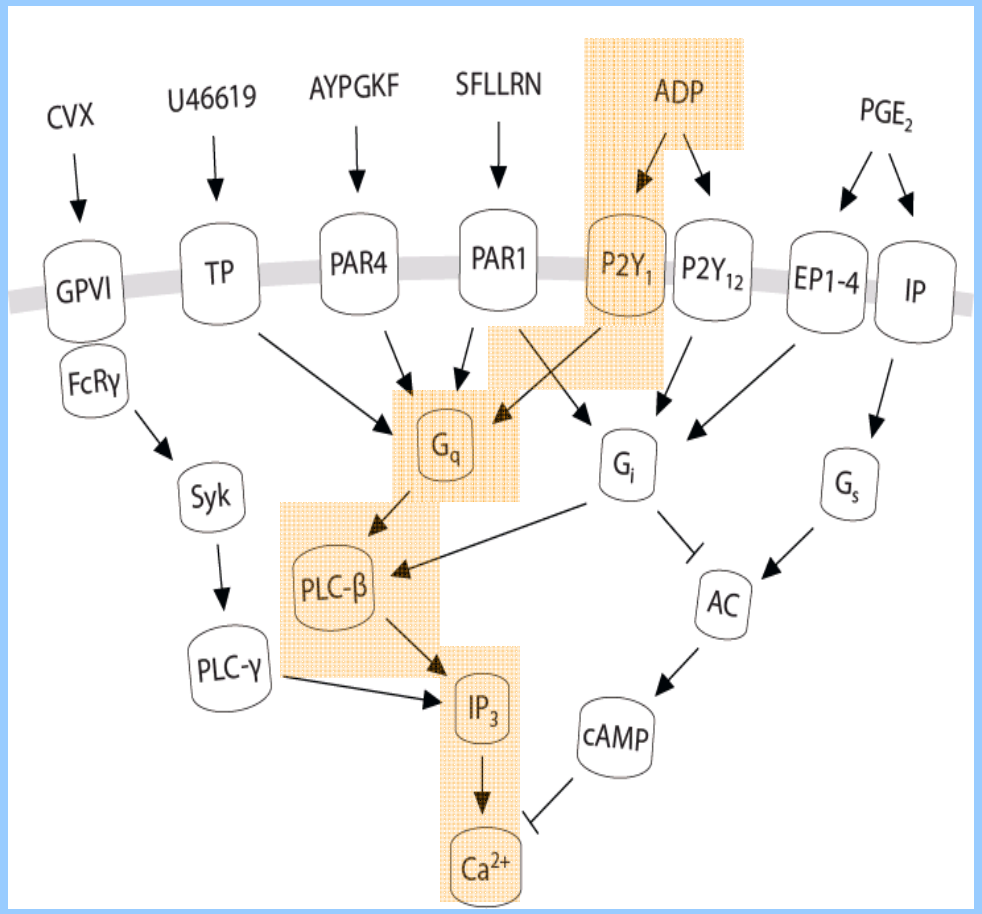


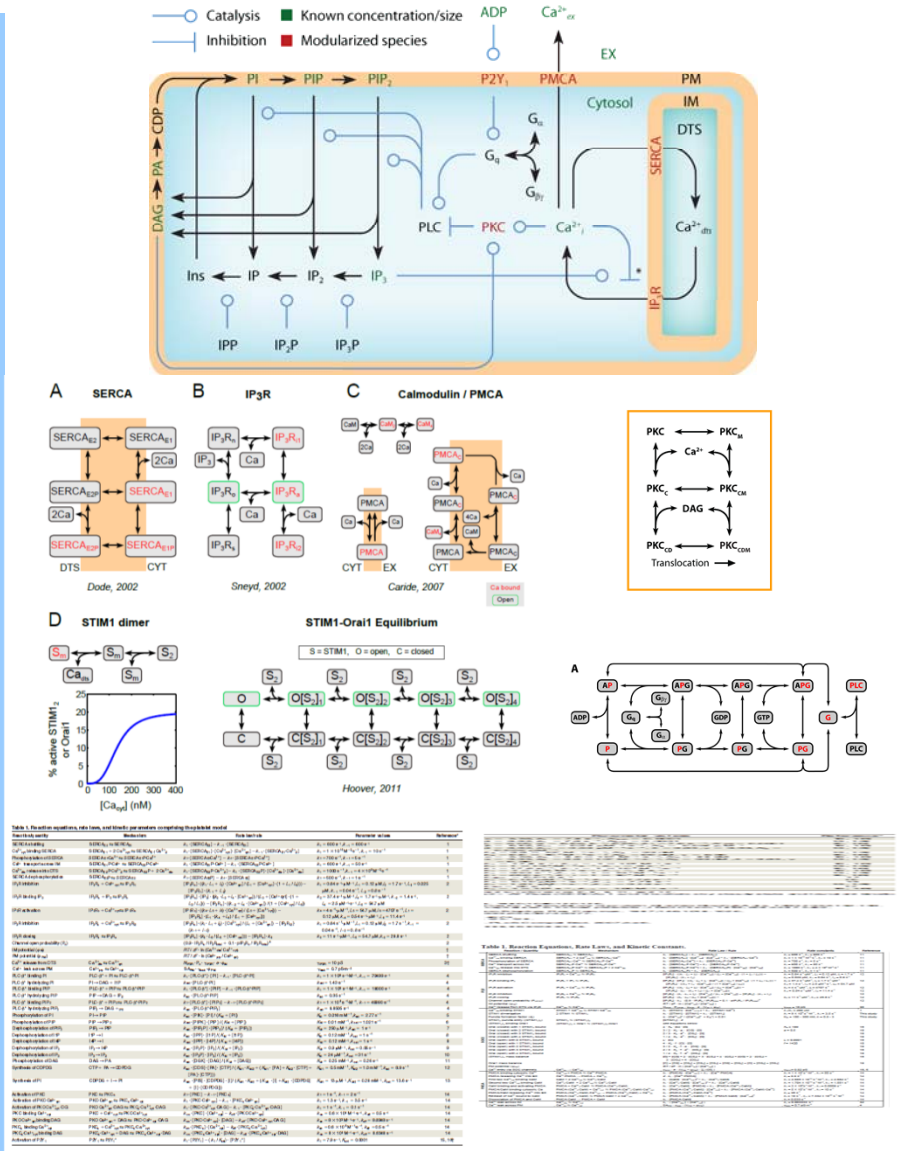
Predictions: ***System evolution $C_i(x,y,z,t)$***

Signaling pathways converging on calcium mobilization



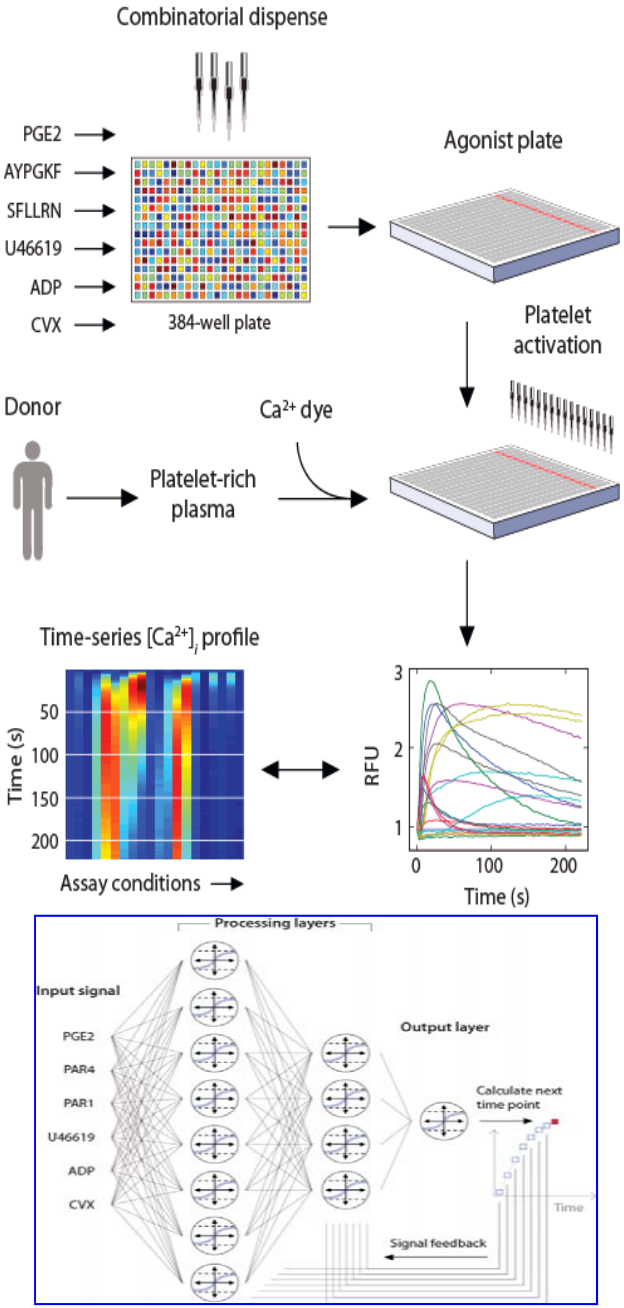
Signaling pathways converging on calcium mobilization

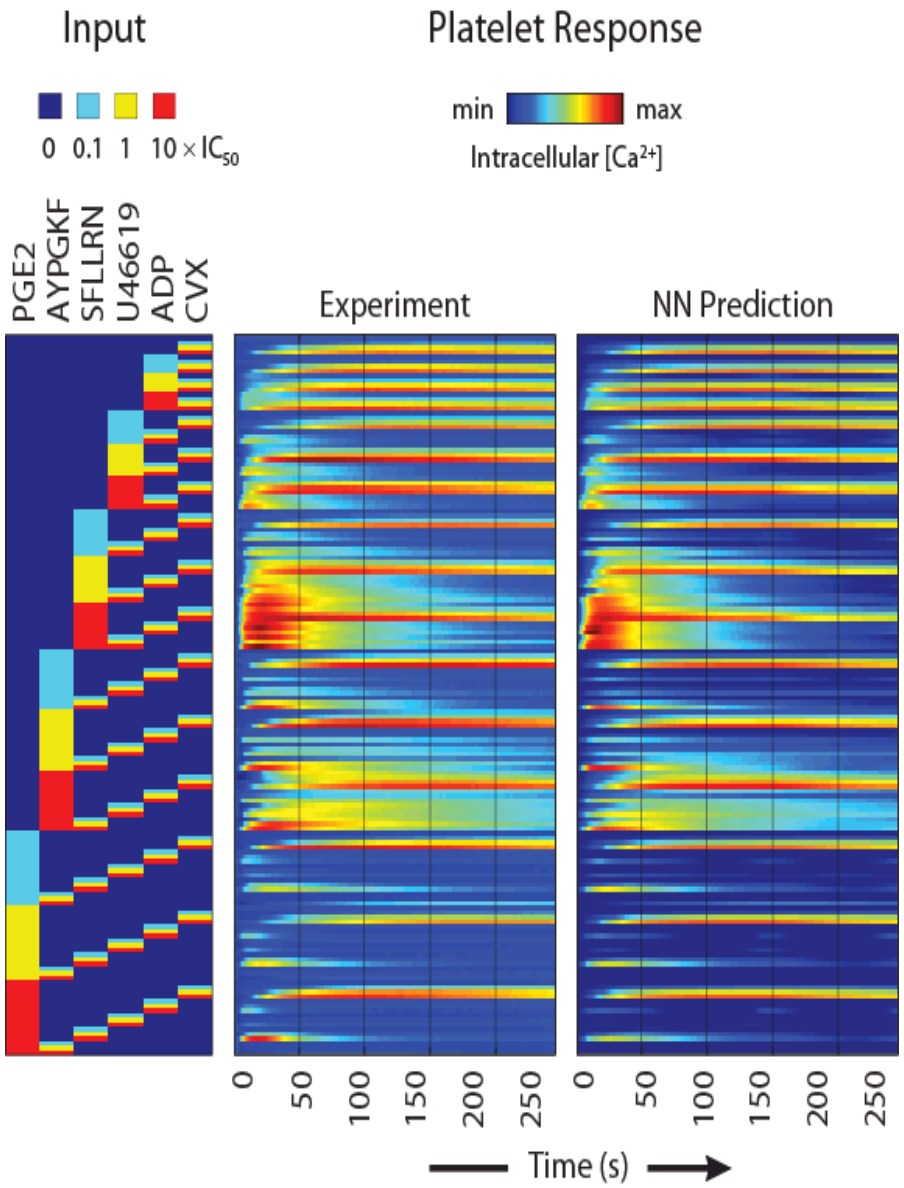




Purvis, et al. *Blood* 2008
Purvis, et al. *PLoS Comp Biol.* 2009
Dolan & Diamond, *Biophys. J.* 2014

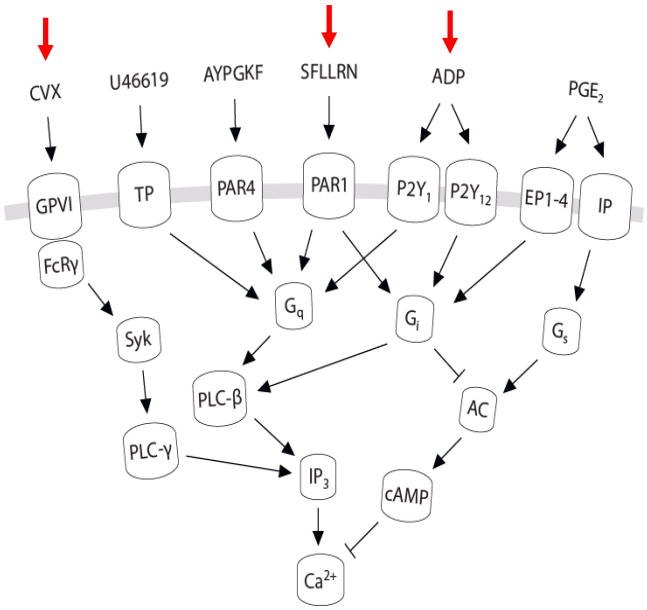
Pairwise Agonist Scanning (PAS)

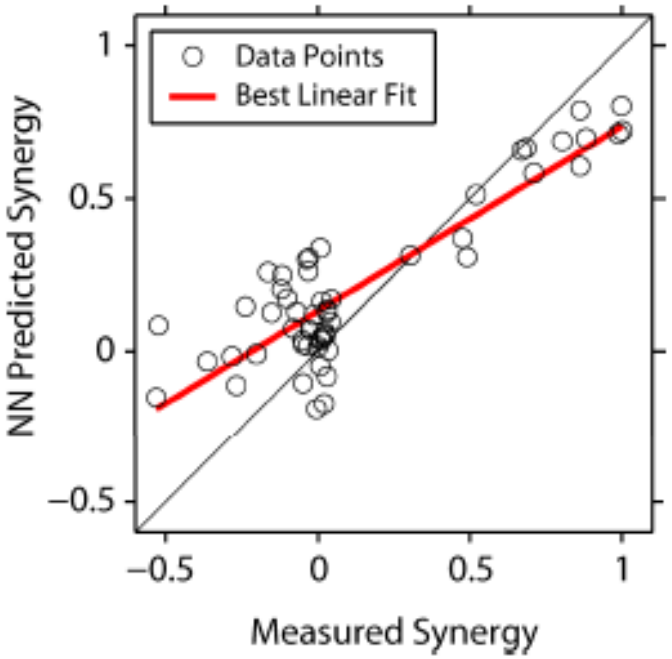


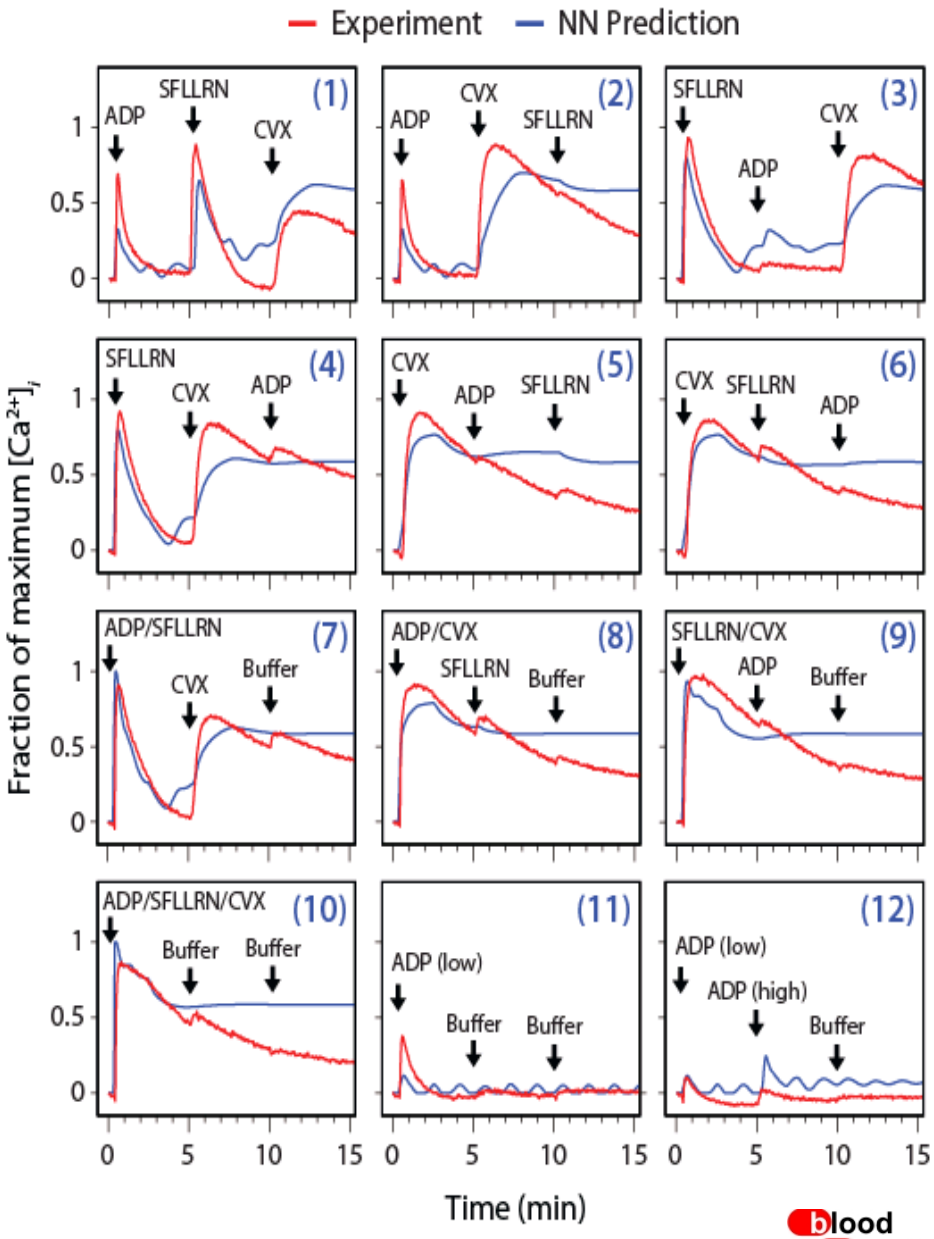


Chatterjee, et al. *Nature Biotechnology* 2010

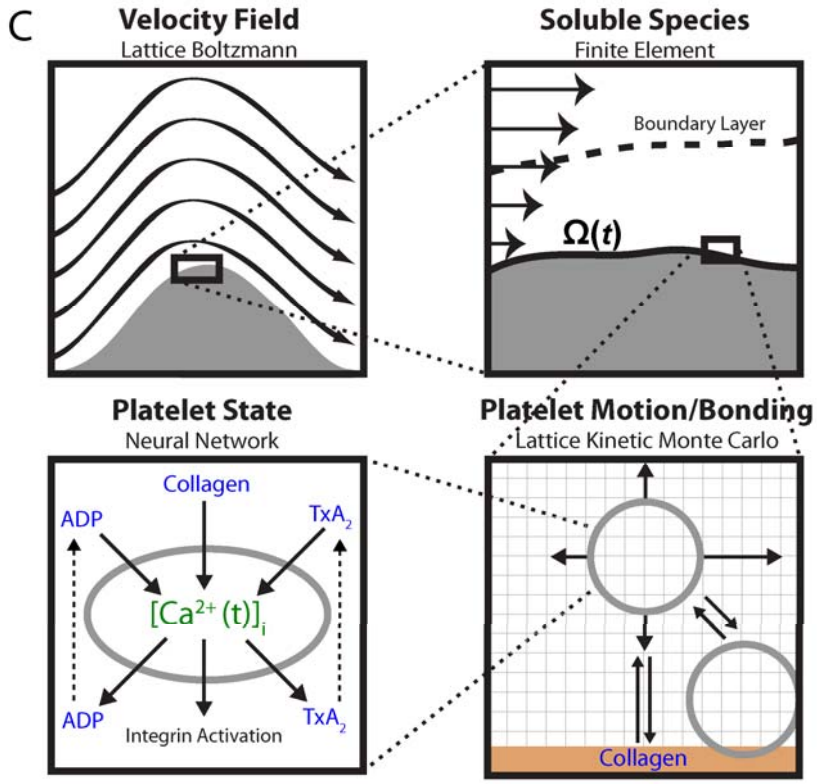
Sequential and ternary addition of: SFFRN, CVX, ADP

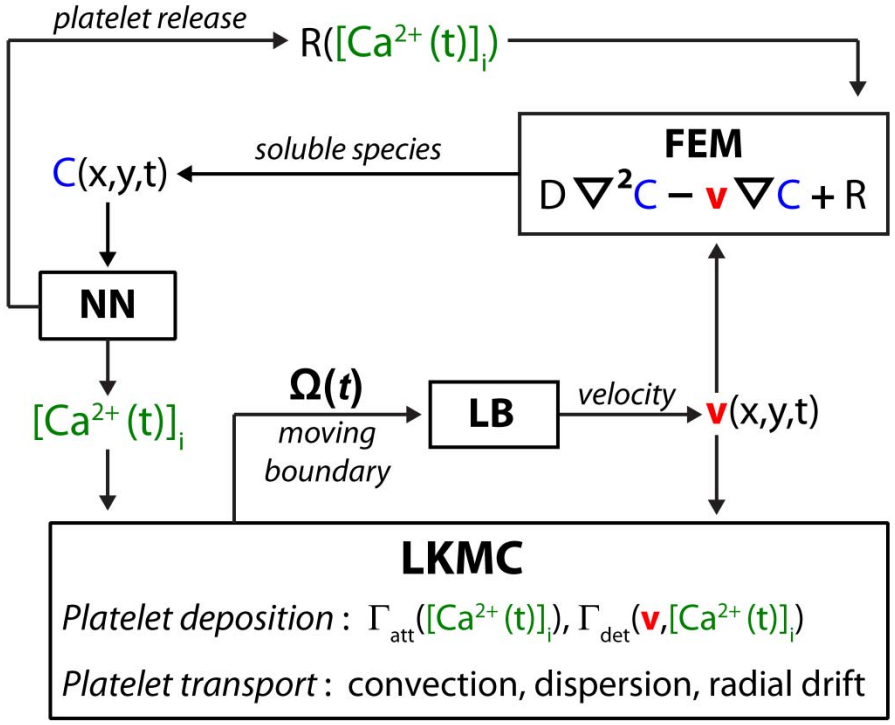






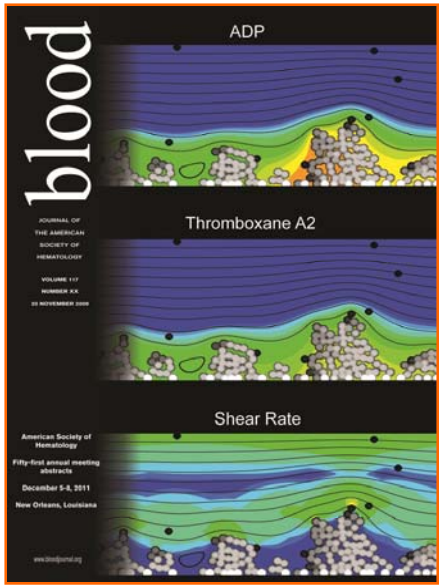
blood systems biology



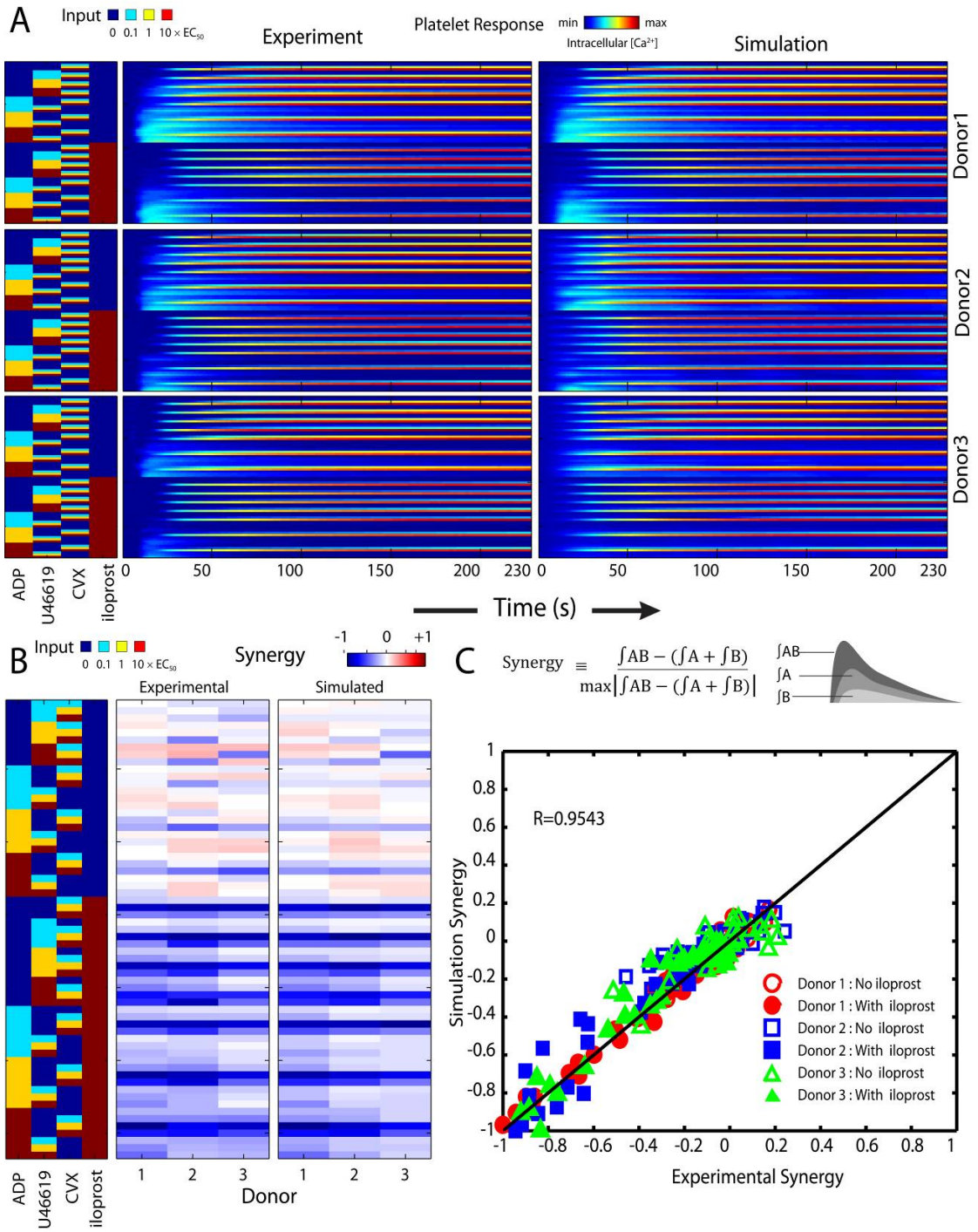


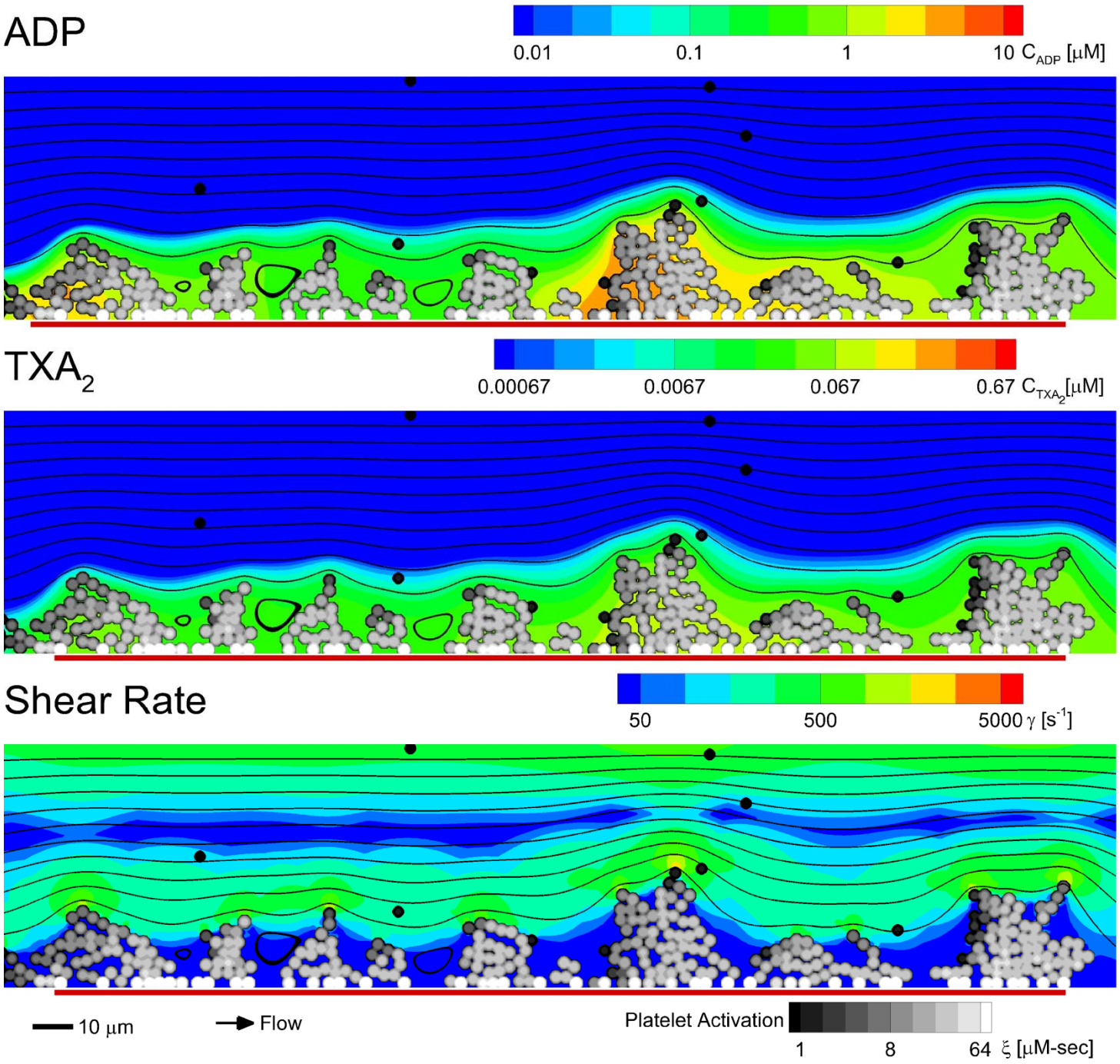
Flamm et al. *J. Chem. Phys.* 2009

Flamm et al. *J. Chem. Phys.* 2011

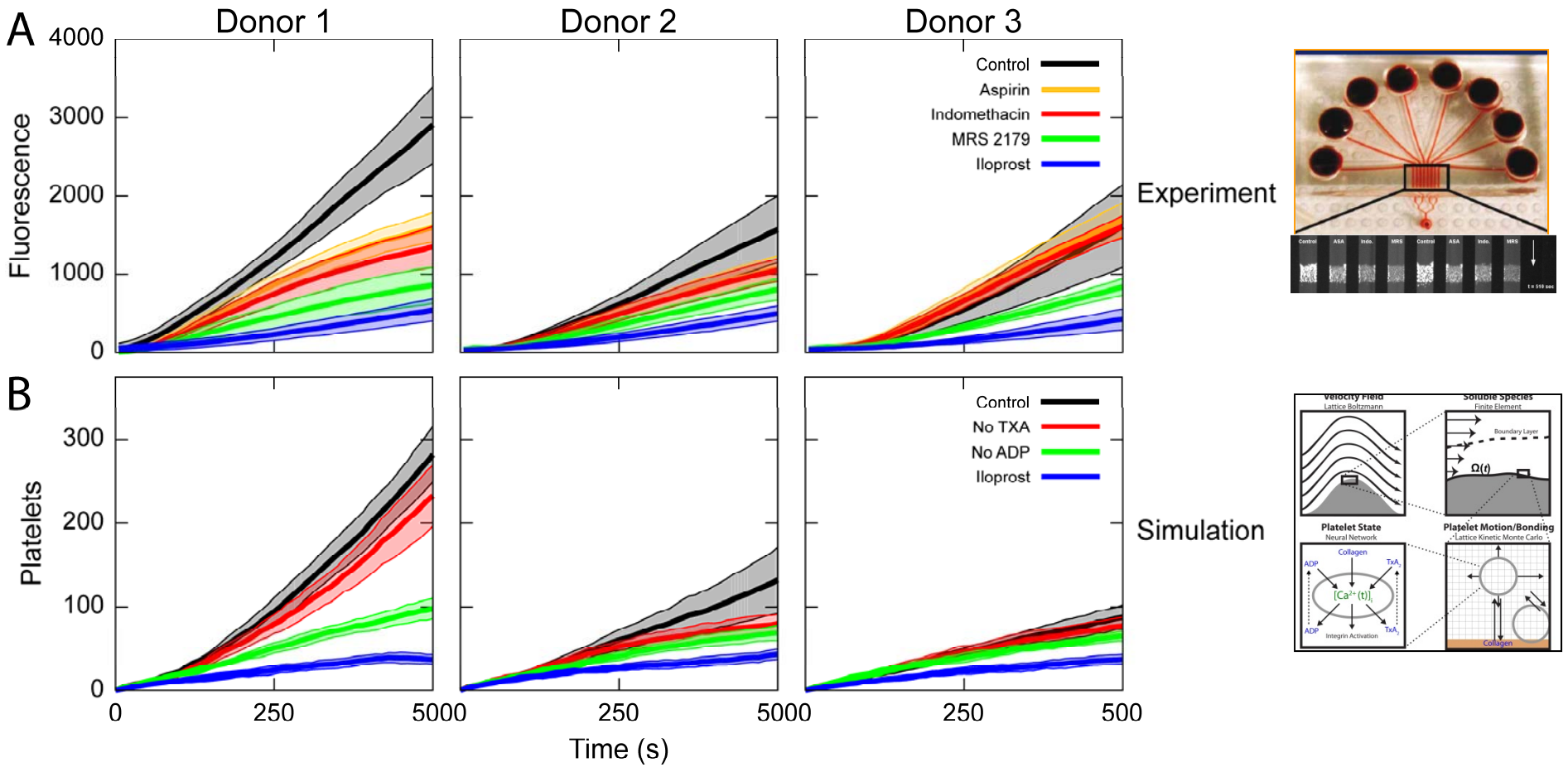


Flamm et al. *Blood*, 2012

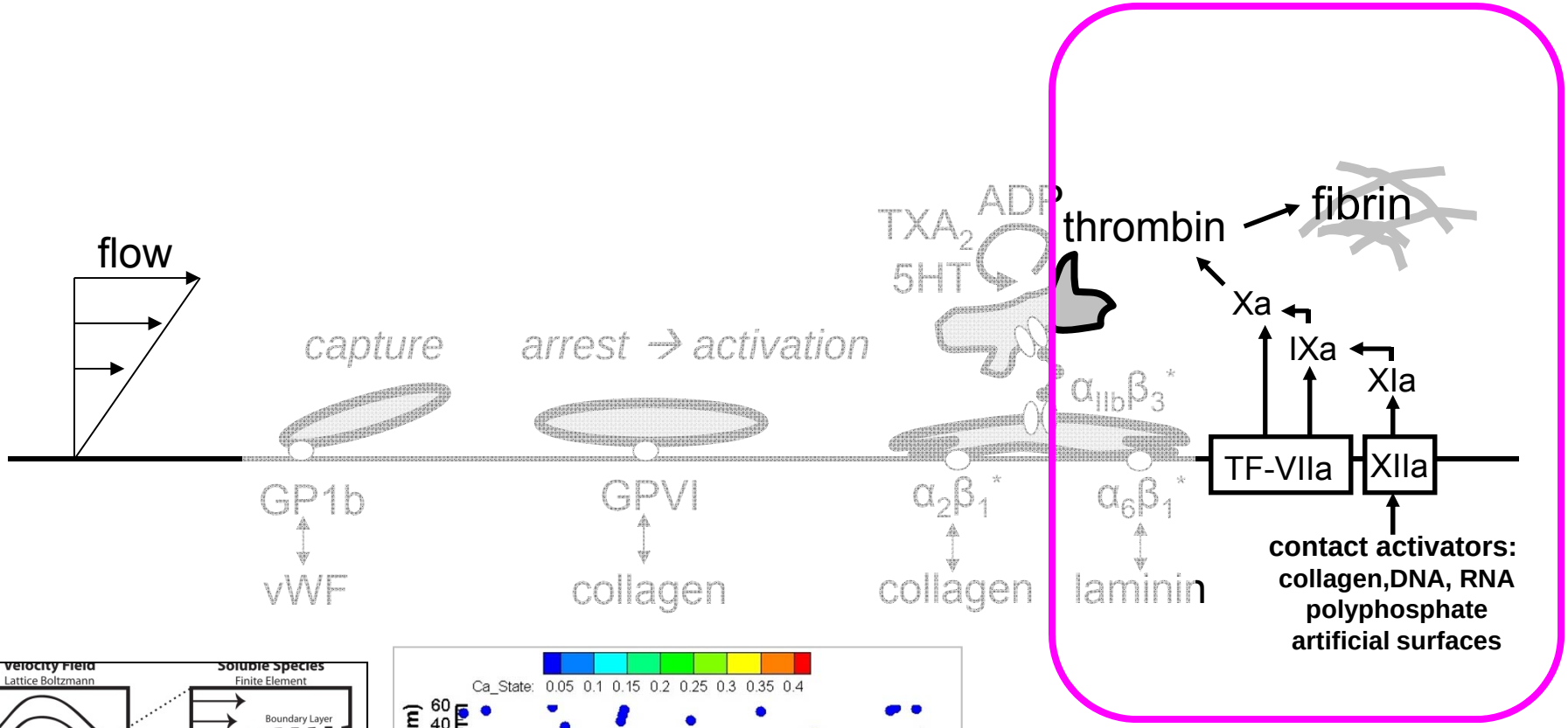


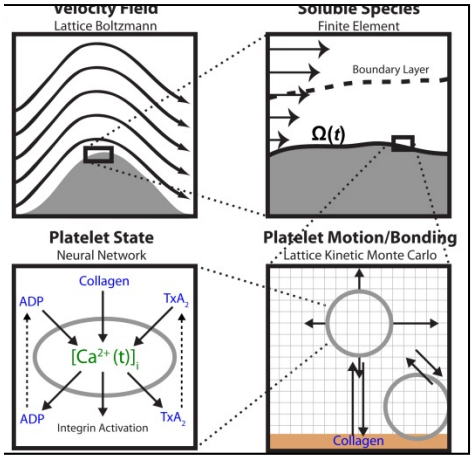

ADP
0.01
0.1
1
10 C_{ADP} [μM]
TXA_2
0.00067
0.0067
0.067
0.67 C_{TXA_2}[μM]
Shear Rate
50
500
5000 γ [s^{-1}]
10 μm
Flow
Platelet Activation
1
8
64 ξ [μM-sec]

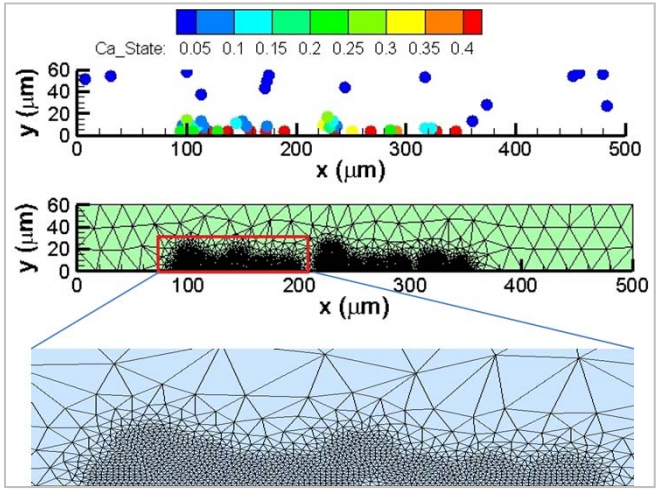
Microfluidic phenotyping of individual subjects (PPACK-whole blood over collagen 200 s^{-1})



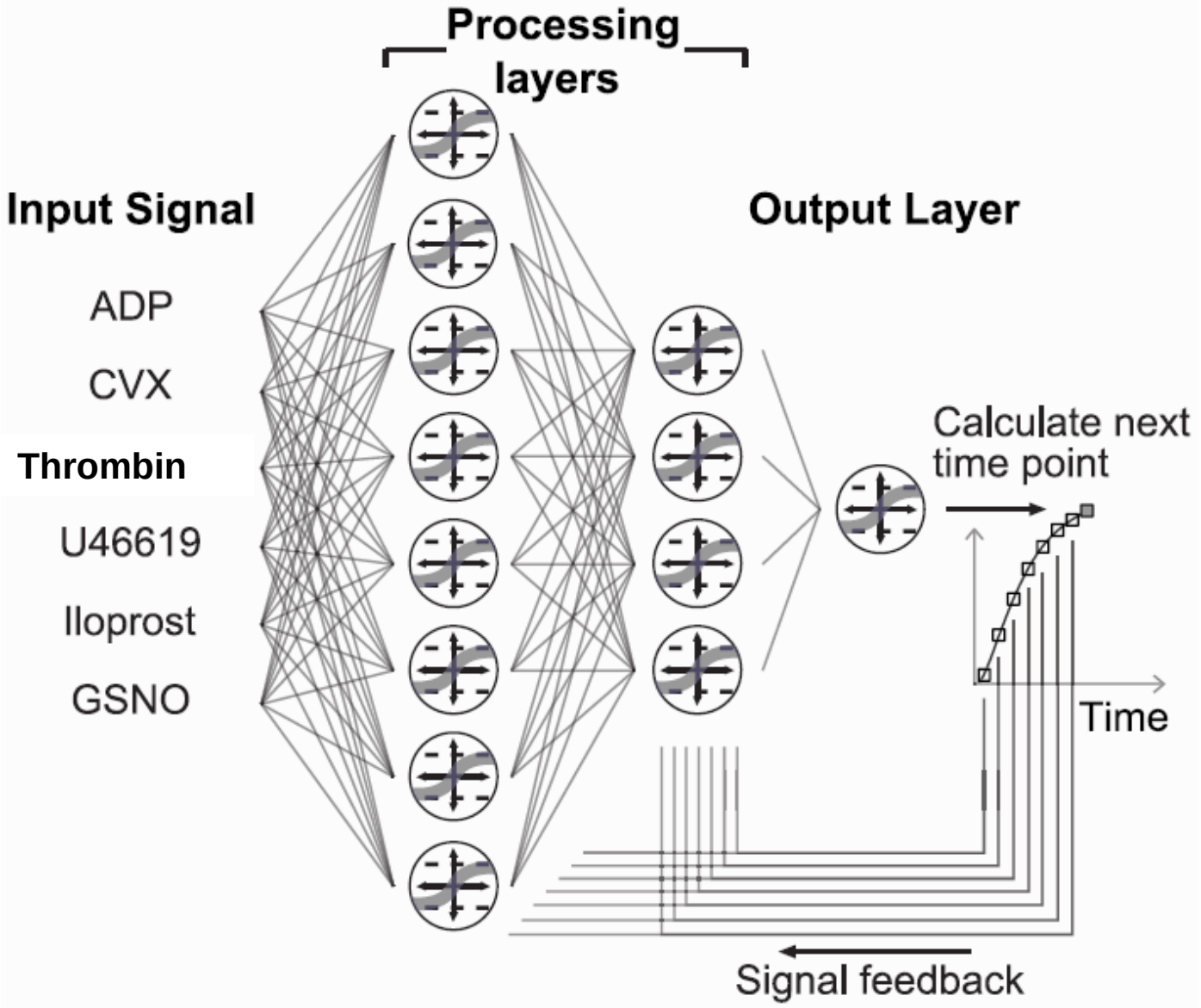
Platelet function during thrombosis and hemostasis





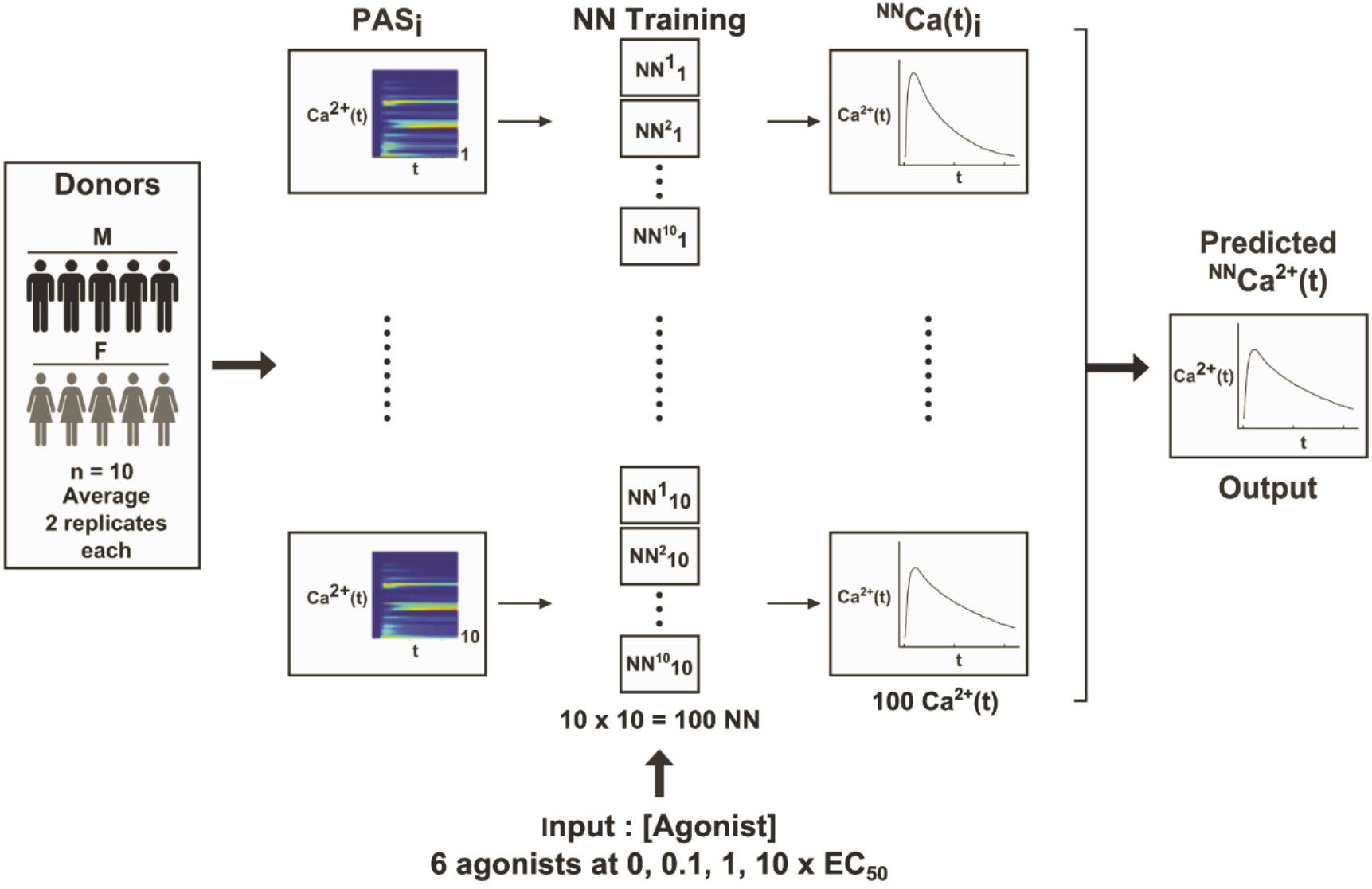


Neural Network Architecture



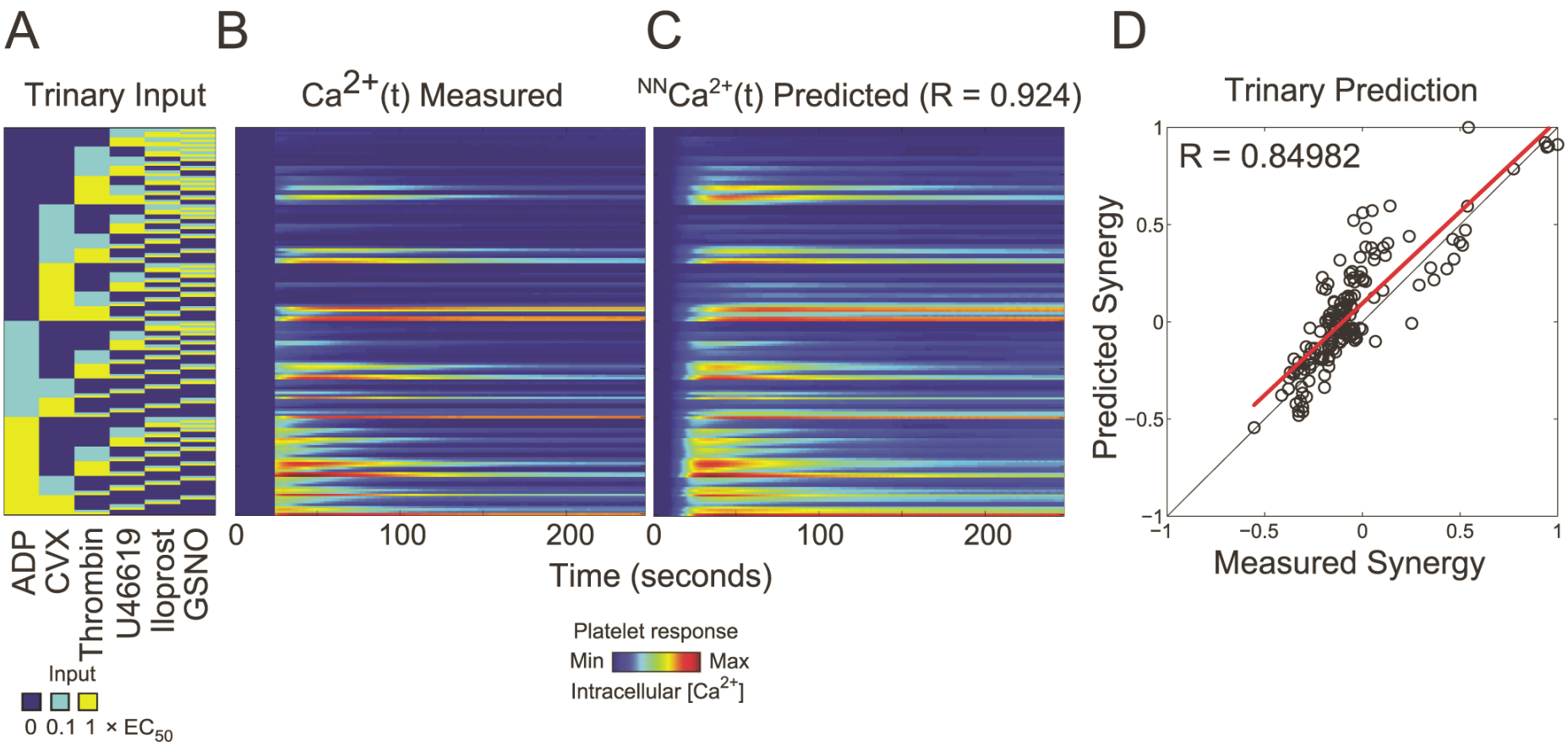
Lee et. al., PLOS Computational Biology., *2015*

Neural Network Architecture

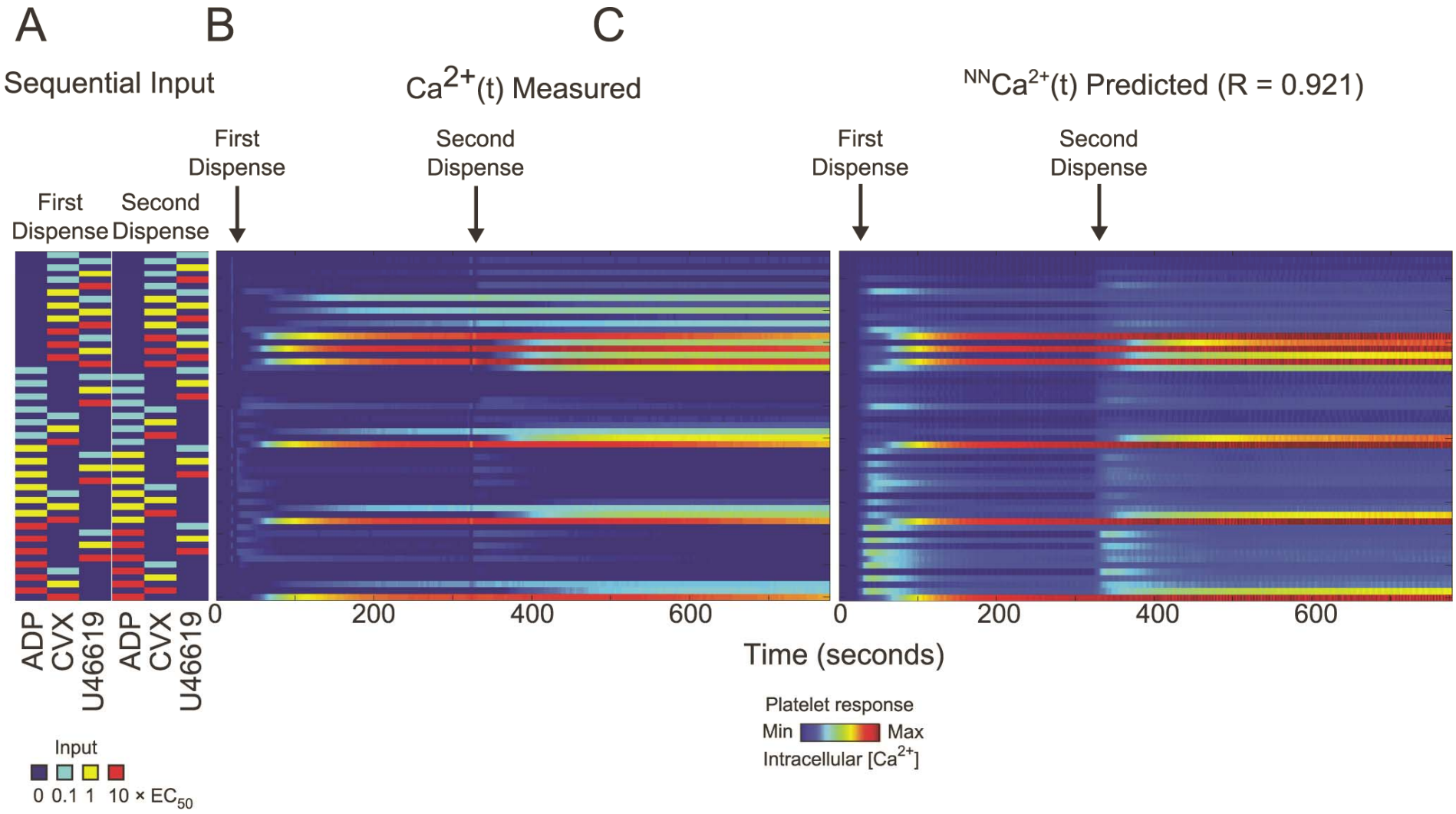


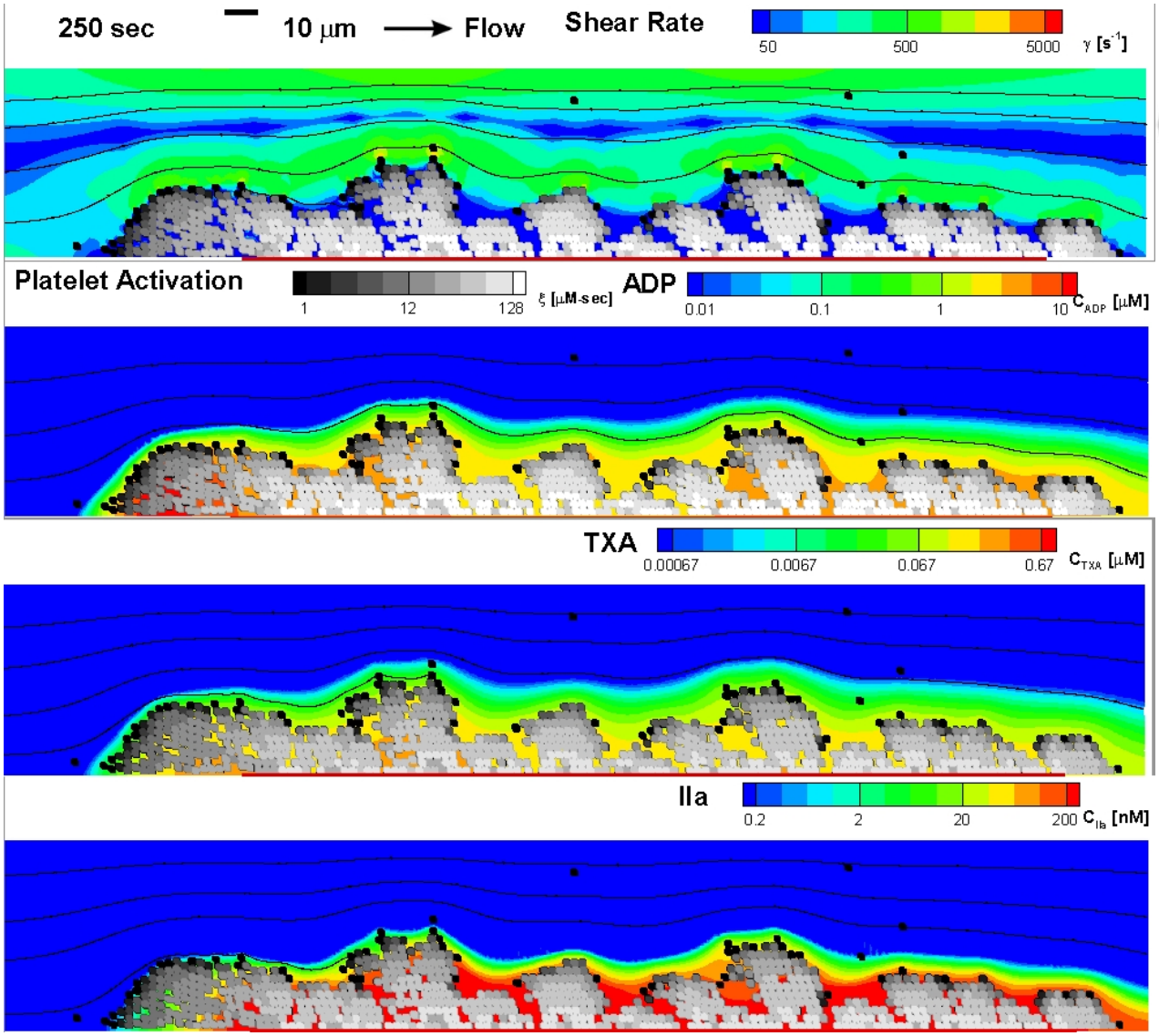
Lee et. al., PLOS Computational Biology., *2015*

Trinary Predictions

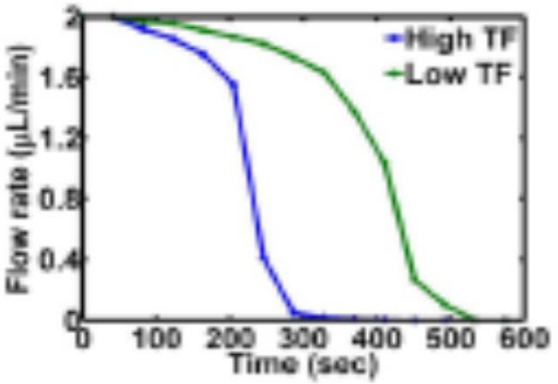


Sequential Exposures - Predictions

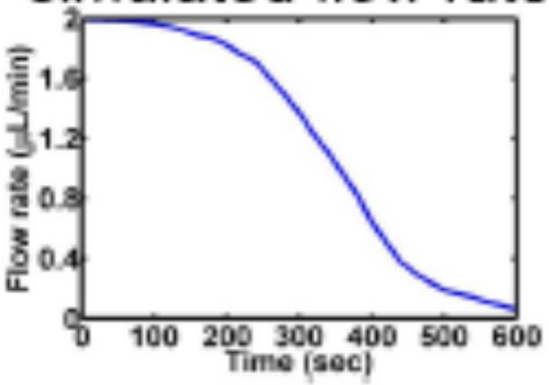




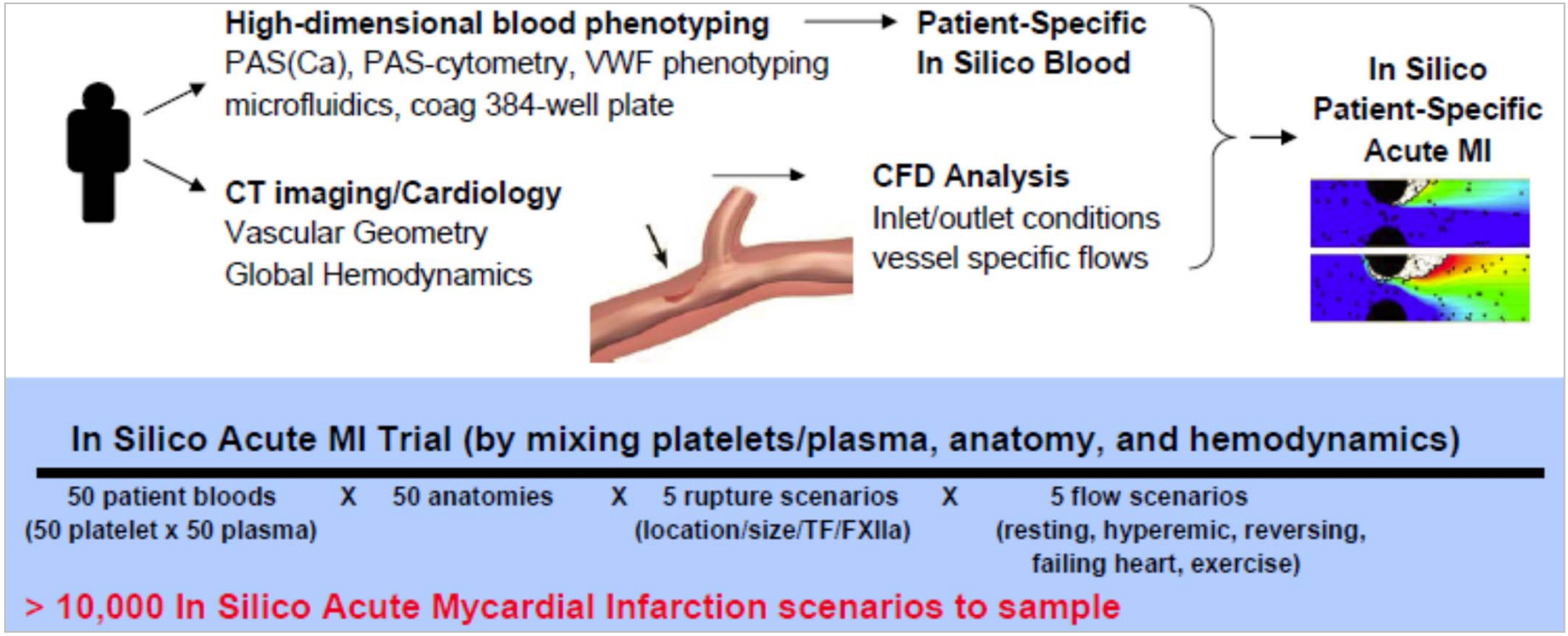
experimental flow rate

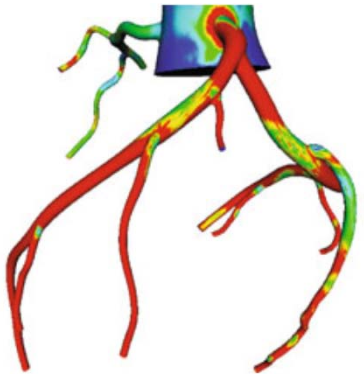


simulated flow rate



Future work: Diagnostics
– acute MI, trauma, hemophilia, neonatal, drug response





Patient-specific Acute MI:
2D → 3D calculations,
Adaptive meshing, GPUs
Parallel processing